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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/530,061	04/04/2005	John Sidney	2060.0330002/EKS/MM	7448

26111 7590 01/14/2008

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.
1100 NEW YORK AVENUE, N.W.
WASHINGTON, DC 20005

EXAMINER	
BRISTOL, LYNN ANNE	

ART UNIT	PAPER NUMBER
1643	

MAIL DATE	DELIVERY MODE
01/14/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/530,061	SIDNEY ET AL.	
	Examiner	Art Unit	
	Lynn Bristol	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 October 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,5-13,18 and 20-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5-13,18 and 20-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1, 5-13, 18 and 20-29 are all the pending claims for this application.

2. Claims 2-4, 14-17 and 19 were cancelled, Claims 1, 5-10 and 13 were amended and new Claims 20-29 were added in the Response of 10/30/07.

3. Claims 1, 5-13, 18 and 20-29 are all the pending claims in this application.

4. Applicants amendments to the claims have necessitated new grounds for objection and rejection. This action is FINAL.

Withdrawal of Objections

Oath/Declaration

5. The objection to the Oath/Declaration of 4/4/05 for containing non-initialed and/or non-dated alterations is withdrawn in view of the copy of the originally filed Oath/Declaration enclosed with the Response of 10/30/07.

Applicants' comments on pp. 9-10 of the Response of 10/30/07 are acknowledged.

Specification

6. The objection to the abstract of the disclosure for being a virtual copy of the cover page from the corresponding WO 2004/031211 application is withdrawn in view of the revised abstract on pp.3-4 and further in view of Applicants' comments on p. 10 of the Response of 10/30/07.

7. The objection to the specification because it does not provide sequence identifiers for the peptide sequences in Tables 5, 6 and 11-29 is withdrawn in view of the amendment of the tables to include SEQ ID NOs.

Applicants' comments and explanation on p. 11 of the Response of 10/30/07 regarding the amendment of Tables 5 and 6 is gratefully acknowledged.

8. The objection to the figure legend to Figure 1 because it does not recite the sequence identifiers for the anchor residues having ≥ four (4) amino acid residues shown in Figure 1 is withdrawn in view of the amendment of the figure legend on p. 3 and further in view of Applicants' explanation on pp. 11-12 of the Response of 10/30/07.

Withdrawal of Rejections

Claim Rejections - 35 USC § 112, second paragraph

9. The rejection of Claims 1, 3-15 and 18 for reciting "peptides" which read on any sequence that comprises the elected peptides or epitopes of SEQ ID NOS: 53, 55, 139, 502, 527, 627, 673, 807, 846 and 859 is with withdrawn and moot for cancelled Claims 3, 4, 14 and 15 and withdrawn for Claims 1, 5-13 and 18 in view of the amendment of Claim 1 to include characteristics of the peptide: residue length, i.e., "thirteen residues or less in length" and the recited peptide species comprising at least one of the peptides of the composition. However, it is the examiner's position that the limitation "thirteen residues or less in length" raises new grounds for rejection as discussed below.

10. The rejection of Claims 3 and 5 for reciting the phrase "HLT epitope" is withdrawn and moot for cancelled Claim 3 and withdrawn for Claim 5 in view of Applicants' detailed explanation on pp. 12-14 of the Response of 10/30/07.

11. The rejection of Claims 3-5 and 8 because it is not clear how the HTL and CTL epitopes and the MHC targeting sequence are related to the peptides of Claim 1 is withdrawn and moot for cancelled claims 3 and 4 and withdrawn for Claims 5 and 8 in view of the amendment of the claims to describe the relationship of the CTL epitope, HTL epitope, and MHC targeting sequence with respect to the overall composition, e.g., being admixed with or linked to the peptides.

Applicants' comments on p. 14 of the Response of 10/30/07 are acknowledged.

12. The rejection of Claims 1, 6, 7 and 9 as being indefinite as to how the "spacer molecule" (Claim 6), "carrier" (Claim 7) and "lipid" (Claim 9) relate to the peptides of the composition of Claim 1 is withdrawn and moot in view of the amended claims.

Applicants' comments on p. 14 of the Response of 10/30/07 are acknowledged.

13. The rejection of Claims 11 and 12 as being indefinite for the recitation "heteropolymer" and "homopolymer" with respect to the overall composition is withdrawn in view of claim 1 having been amended to more clearly recite the peptide structures and further in view of Applicants' allegations on pp. 14-15 of the Response of 10/30/07.

Claim Rejections - 35 USC § 112, first paragraph

Enablement

14. The rejection of Claims 3 and 4 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement is withdrawn and moot in view of the cancelled claims.

15. The rejection of Claims 14 and 15 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement as being drawn to a pharmaceutical composition with an intended use to prevent a disease or disorder (Claim 14) and a vaccine composition (Claim 15) is withdrawn and moot in view of the cancelled claims.

Applicants' comments on p. 19 are acknowledged.

Rejections Maintained

Enablement

16. The rejection of Claims 5, 8, 11 and 12 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement is maintained.

Applicants' allegations of on pp. 16-18 of the Response of 10/30/07 have been considered but are not found persuasive. Applicants allege that the claims are directed to a composition comprising peptides and that the claims do not require functional limitations or features; the specification teaches how to make compositions comprising the elected peptides (citing ¶¶61-75 of the specification) and to test the compositions in various binding assays (citing ¶77 and 78), and to test the efficacy of the compositions

to determine the capacity to bind to certain MHC molecules and/or to have the ability to induce an immune response.

The examiner respectfully submits that inasmuch as the claims do not recite a function per se, the recitation for a "CTL epitope" impliedly requires that each peptide actually possess the inherent property of being T-cell specific and CTL immunogenic and further as defined in the specification as having MHC binding ability. Applicants' arguments that no functional meaning or interpretation can be read into the claimed composition is inconsistent with their own claim language and definitions provided in the specification. The specification teaches [0036]:

> "The epitopes present in the invention can be dominant, sub-dominant, or cryptic. A dominant epitope is an epitope that induces an immune response upon immunization with a whole native antigen. See, e.g., Sercarz, et al., Ann. Rev. Immunol. 11: 729-766 (1993). Such a peptide is considered immunogenic because it elicits a response against the whole antigen. A subdominant epitopes, on the other hand, is one that evokes little or no response upon immunization with whole antigen that contains the epitope, but for which a response can be obtained by immunization with an isolated epitope. Immunization with a sub-dominant epitope will prime for a secondary response to the intact native antigen. A cryptic epitope elicits a response by immunization with an isolated peptide, but fails to prime a secondary response to a subsequent challenge with whole antigen" ,

and at [0069]:

> "The peptides of the present invention or analogs thereof which have CTL and/or HTL stimulating activity may be modified to provide desired attributes other than improved serum half life",

and in the Abstract:

> "Peptides...as capable of binding one or more MHC molecules and inducing an immune response in a system",

and at [0014]:

> "As used herein, the term "peptide" is used interchangeably with "epitope" in the present specification to designate a series of residues, typically L-amino acids, connected one to the other, typically by peptide bonds between the .alpha.-amino and carboxyl groups of adjacent amino acids, that binds to a designated MHC allele."

The examiner further submits that the claimed compositions are required to possess both CTL and HTL immunogenic properties (Claim 5) or CTL immunogenic properties and MHC targeting ability (Claim 8), and further that any one of the CTL-inducing peptides could be in the form of a heteropolymer or homopolymer and still retain the CTL and MHC activities (Claims 11 and 12). It is not understood how one of ordinary skill in the art in reading the specification could possibly conclude that the peptides were not required to possess an immunogenic function, more especially in view of the instant claimed required feature of being a "CTL epitope" in addition to any other features required of the rejected claims. (MPEP 2106, *E-Pass Techs., Inc. v. 3Com Corp.*, 343 F.3d 1364, 1369, 67 USPQ2d 1947, 1950 (Fed. Cir. 2003) (claims must be interpreted "in view of the specification" without importing limitations from the specification into the claims unnecessarily).

Applicants' allege despite the fact that experimentation may be complex does not make it undue if the art typically engages in such experimentation as for the instant case; and that no experimentation is necessary to practice the invention.

The examiner respectfully submits that the specification would provide the steps for making and screening the CTL epitopes for the ordinary skilled artisan at the time of the invention, but that based on the field of art as whole, the generation of immunogenic peptides was unpredictable. Thus experimentation would have been required to test the compositions for the various peptides and recited combinations to determine whether they possessed a) CTL immunogenic activity and MHC binding or b) HTL immunogenic activity and MHC binding.

Applicants do not appear to appreciate the cited references (Schirle et al. (J. Immunol. Methods. 2001; 257: 1-16); Anderson et al. (Tissue Antigens. 2000 Jun; 55 (6): 519-531); Feltkamp et al. (Mol. Immunol. 1994 Dec; 31 (18): 1391-1401); Beier et al. (USPN 2004/0037840; published 2/26/2004; filed 10/26/2001)) for their general discussion regarding the poor correlation between predicted and experimental results for immunogenic peptides at the time of filing. (MPEP 2164.02 "However, in applications directed to inventions in arts where the results are unpredictable, the disclosure of a single species usually does not provide an adequate basis to support generic claims. In re Soll, 97 F.2d 623, 624, 38 USPQ 189, 191 (CCPA 1938). In cases involving unpredictable factors, such as most chemical reactions and physiological activity, more may be required. In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) (contrasting mechanical and electrical elements with chemical reactions and

physiological activity). See also In re Wright, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993); In re Vaeck, 947 F.2d 488, 496, 20 USPQ2d 1438, 1445 (Fed. Cir. 1991). This is because it is not obvious from the disclosure of one species, what other species will work").

New Grounds for Rejection

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Written Description

17. Claims 1, 5-13, 18 and 20-29 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 1, 5-13, 18 and 20-29 recite matter that was not described in the original specification or original claims.

Claims 1, 5-13, 18 and 20-29 are interpreted as being drawn to a composition comprising one or more peptides "thirteen residues or less in length", wherein at least one or more peptides comprises a CTL epitope (Claim 1) and where an HTL peptide "is less than 50 residues in length" (claim 5).

The limitations "thirteen residues or less in length" and "less than 50 residues in length" find per se support in [0041] of the specification where it states:

"One embodiment of an HTL-inducing peptide is *less than about 50 residues in length* and usually consist of between about 6 and about 30 residues, more usually between about 12 and 25, and often between about 15 and 20 residues, for example 15, 16, 17, 18, 19, or 20 residues. One embodiment of an CTL-inducing peptide is *13 residues or less in length* and usually consists of about 8, 9, 10 or 11 residues, preferably 9 or 10 residues.

And at [0038] of the specification: "The epitopes of the present invention can be any suitable length. Class I molecule binding peptides typically are about 8 to 13 amino acids in length, and often 9, 10, 11, or 12 amino acids in length."

It is the examiner's position that both limitations could encompass peptides as small as 2 amino acids in length, where a peptide is known in the art and defined as "A compound of two or more amino acids in which a carboxyl group of one is united with an amino group of another, with the elimination of a molecule of water, thus forming a peptide bond, –CO–NH–; i.e., a substituted amide" (see Stedman's Medical Dictionary, 27th Ed.). Thus in view of the art-recognized meaning of a peptide, the instant claimed ranges of peptide sizes, and the specific teachings in the specification for de minimus sizes of CTL-epitopes and HTL epitopes, it is not at all apparent that Applicants specification discloses examples of immunogenic peptides being less than the preferred disclosed ranges, for example in [0041].

The specification does not provide sufficient written description as to the structural features of the claimed genus of CTL peptides "*thirteen residues or less*" or the HTL peptides "*less than about 50 residues in length*", and the correlation between the chemical structure and function of the genus of peptides falling within these size range, such as structural domains or motifs that are essential and distinguish members of the genus from those excluded. Applicants specification describes preferred size ranges comprising the minimal essential motifs which retain biological activity but the claimed ranges encompass species that are not defined.

A "representative number of species" means that the species, which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. The disclosure of only one species encompassed within a genus adequately describes a claim directed to that genus only if the disclosure "indicates that the patentee has invented species sufficient to constitute the gen[us]. " See Enzo Biochem, 323 F.3d at 966, 63 USPQ2d at 1615; Noelle v. Lederman, 355 F.3d 1343, 1350, 69 USPQ2d 1508, 1514 (Fed. Cir. 2004) (Fed. Cir. 2004)("[A] patentee of a biotechnological invention cannot necessarily claim a genus after only describing a limited number of species because there may be unpredictability in the results obtained from species other than those specifically enumerated."). "A patentee will not be deemed to have invented species sufficient to constitute the genus by virtue of having disclosed a single species when ... the evidence indicates ordinary artisans could not predict the operability in the invention of any species other than the

one disclosed." In re Curtis, 354 F.3d 1347, 1358, 69 USPQ2d 1274, 1282 (Fed. Cir. 2004)(Claims directed to PTFE dental floss with a friction-enhancing coating were not supported by a disclosure of a microcrystalline wax coating where there was no evidence in the disclosure or anywhere else in the record showing applicant conveyed that any other coating was suitable for a PTFE dental floss.).

It has been well known that minor structural differences even among structurally related compounds can result in substantially different biology, expression and activities. Based on the instant disclosure one of skill in the art would not know which sequences are essential, which sequences are non-essential and what particular sequence lengths identify essential sequences for identifying a CTL or HTL peptide encompassed by the claimed specificity. Mere idea of function is insufficient fro written description; isolation and characterization at a minimum are required.

Scholnick et al (Trends in Biotechnology, 18(1):34-39, 2000) teach that the skilled artisan is well aware that assigning functional activities for any particular protein or protein family based on sequence homology is inaccurate, in part because of the multifunctional nature of proteins (e.g., "Abstract" and "Sequence-based approaches to function prediction", page 34). Even in situations where there is some confidence of a similar overall structure between two proteins, only experimental research can confirm the artisan's best guess as to function of the structurally related protein (see in particular "Abstract" and Box 2).

For inventions in an unpredictable art as in the instant case, adequate written description of a genus, which embraces widely variant species cannot be achieved by

disclosing only one species within the genus. In the instant case, applicant has not even disclosed a single species, e.g., peptide varying in length from 2-6 amino acids, encompassed by the highly variant genus nor is there disclosure of the common attributes or features (i.e., structural domains) that are essential for activity or those which are non-essential. See, e.g., Eli Lilly. Description of a representative number of species does not require the description to be of such specificity that it would provide individual support for each species that the genus embraces. If a representative number of adequately described species are not disclosed for a genus, the claim to that genus must be rejected as lacking adequate written description under 35 U.S.C. 112, first paragraph.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of CTL peptide falling within the range of "*thirteen residues or less*" or the HTL peptides "*less than about 50 residues in length*", and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of

isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddles v.Baird*, 30 USPQ2d 1481, 1483. In *Fiddles v. Baird*, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Conclusion

18. No claims are allowed.

19. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lynn Bristol whose telephone number is 571-272-6883. The examiner can normally be reached on 8:00-4:00, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on 571-272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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LARRY R. HELMS, PH.D.
SUPERVISORY PATENT EXAMINER